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AUG 24 2006

Application No.: 09/914,795
Inventor: BERNDL et al.
Reply to Office Action of 24 May 2006
Docket No.: 49727

REMARKS/ARGUMENTS

Claim 2-8 are pending. Claim 1 has been canceled, claims 2-3, 5-6 and 8 have been amended, and claim 9-18 have been added. Claims 2-7 are now dependent from amended claim 8. Support for amended claim 8 can found in the claims as originally submitted. Support for claims 9-18 can be found in the original claims and in the specification. More specifically, support for the new claims can at least be found in the specification or the original claims in the following pages and/or claims: Claim 9, page 12, lines 17-25; Claim 10, page 12, line 21-28; Claim 11, original claim 5; Claim 12, page 4, line 41, page 5, lines 3-6, page 9, lines 21-23, page 15, line 17, and Example 2; Claim 13, page 7, lines 7-24; Claim 14, page 6, 17-20; Claim 15, page 7, lines 24-28; Claim 16, page 4, line 7; Claim 17, page 3, line 27; and Claim 18, page 3, lines 24-25. No new matter has been entered and no new issues are raised with these amendments.

Remarks regarding the rejection under 35 USC §112 ¶2

Claims 1-8 stand rejected as allegedly indefinite. The Examiner asserts that the phrase "accelerated release" is indefinite. Applicants respectfully disagree but have cancelled claim 1, wherein said phrase appeared, in order for a more speedy prosecution of the instant application. Accordingly, the 112 rejection is moot and withdrawal of the rejection is respectfully requested.

Remarks regarding the rejection under 35 USC §102

Claims 1-7 stand rejected as allegedly anticipated by EP 0564945. Applicants canceled claim 1 and amended claims 2-7 to depend from amended claim 8. Accordingly, because claim 1 has been canceled and because claims 2-7 depend from claim 8; which stands free of anticipation, the rejection is moot. Applicants respectfully request withdrawal of the 102 rejection.

Remarks regarding the rejection under 35 USC §103

Claim 1-8 stand rejected as allegedly unpatentable in light of US 6,365,188 in view of US

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Application No.: 09/914,795
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Docket No.: 49727

4,801,460. Applicants respectfully disagree.

To establish *prima facie* obviousness, the Examiner must show in the prior art some suggestion or motivation to make the claimed invention, a reasonable expectation for success in doing so, and a teaching or suggestion of each Claim element (See, e.g., *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ 2d 1941 (Fed. Cir. 1992); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). Most inventions arise from a combination of old elements and each element may often be found in the prior art (*In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998)). However, mere identification in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole (*Id.* at 1355, 1357). Rather, to establish a *prima facie* case of obviousness based on a combination of elements disclosed in the prior art, the Examiner must articulate the basis on which it concludes that it would have been obvious to make the claimed invention (*Id.*). In practice, this requires that the Examiner "explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious" (*Id.* at 1357-59). This entails consideration of both the "scope and content of the prior art" and "level of ordinary skill in the pertinent art" aspects of the *Graham* test.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be suggested by the prior art (See, *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). Applicants respectfully assert the cited art references fail to teach all the limitations of the instant claimed invention. The cited art fails to teach at least the following:

- 1) mixing and plasticizing ... at a temperature below 170°C
- 2) 50 to 98% by weight of the at least one polymeric binder

The Examiner acknowledges that US 6,365,168 fails to disclose plasticizing at a temperature below 170°C and a polymeric binder of the present invention (See, 24 May 2006 Office Action, page 5). The Examiner asserts that although a temperature of 239°C is exemplified, US 6,365,168 discloses that different temperatures may be applied as well as the method of ascertaining the required temperature (*Id.* at page 4). Applicants respectfully assert

Application No.: 09/914,795
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that US 6,365,168 cannot reasonably suggest to one of ordinary skill in the art to modify, with the expectation for success, the art reference because disclosure of a temperature of 239°C fails to teach, suggest or disclose a temperature below 170°C as presently claimed.

A proper obviousness analysis requires the recognition that the prior art, not hindsight knowledge of a patentee's success, must motivate a person skilled in the art to do what the patentee has done. (*See, Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000) (citing *In re Rouffet*, 149 F.3d 1350, 1357-58 (Fed. Cir. 1998)). In column 3, line 19, US 6,365,168 states "... at the temperatures needed to melt and extrude the mixture of said one or more active ingredients with a cyclodextrin or cyclodextrins." Thus, the skilled artisan is directed therefrom that the known process is carried out at a temperature close to the melting point of the cyclodextrin or the active ingredient. The Examiner refers to column 4, lines 15-25, "... until melting of one of the components." Applicants respectfully assert that any meaningful interpretation of the expression "one of the components" to the skilled artisan can only refer to one of the disclosed required components, i.e. one of the active ingredients and/or cyclodextrin. It would be inappropriate hindsight interpretation on the Examiner's part to broaden the meaning of "one of the components" to include materials, such as the polymeric binder of the present invention, that are not envisaged in US 6,365,188. Consequently, because it would require hindsight interpretation to include a polymeric binder as "one of the components," US 6,365,168 fails to teach, suggest or disclose a polymeric binder as recited in the invention.

As explained above, on proper interpretation, US 6,365,188 requires working at a temperature at or close to the melting temperature of the cyclodextrin or active ingredient. Such temperatures are disadvantageous in as much as they may cause thermal decomposition of the active ingredient(s) or cyclodextrins. In the present invention, a polymeric binder is included in the melt-extruded mixture. The presence of the polymeric binder significantly lowers the melting point of the mixture and the melt of the polymeric binder acts as a "solvent." Concurrently, the cyclodextrin/active ingredient complex is embedded in the polymeric binder.

Moreover, despite the fact that in column 3, lines 33-40, US 6,365,188 states

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Application No.: 09/914,795
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[m]elt-extrusion is a polymer extrusion technique which involves embedding an active ingredient in one or more carriers. In this technique the active ingredient and the excipients are molten in the extruder and hence embedded in thermoplastic and thermoplastic polymers. The resultant molten mass is then forced through one or more nozzles resulting in a thermoplastic strand or strands.

The above disclosed procedure is a mere explanation of the term "melt-extrusion." This explanation is given with reference to conventional melt-extrusion techniques that use thermoplastic polymers. The reference to thermoplastic polymers is, however, unrelated to the invention disclosed in US 6,365,168. In fact, whereas US 6,365,168 refers to thermoplastic polymers in the discussion of the term "melt-extrusion," the remainder of the art reference is silent on thermoplastic polymeric binders. Accordingly, Applicants respectfully assert that one of ordinary skill in the art would conclude that the incorporation of such polymers would be considered inapposite to the disclosure of the inventors of US 6,365,188.

Further still, the Examiner asserts that the mixture of US 6,365,188 may contain additives such as polyethylene glycol. Whereas the art reference does not state an upper limit for the amount of such additives, Applicants respectfully assert that these additives, such as pigments, flavors, stabilizers, preservatives, buffers and plasticizers, are conventionally used in extremely small amounts. For example, the art reference discloses an amount of 100-5000 ppm of anti-oxidizing agent. Contrary thereto, the instant invention requires 50-98% by weight of polymeric binder, an amount well above the range in which ordinary additives are used and contrary to that which is disclosed in the art. Accordingly, one of ordinary skill in the art would fail to be motivated to modify the additives of US 6,365,188 from a ppm range to a range of 50-98% by weight with the expectation for success to practice the instant invention.

Turning now to US 4,801,460. This art reference discloses a process for the preparation of a solid pharmaceutical form by mixing a pharmaceutically active compound with a fusible pharmalogically tolerated binder and subjecting the mixture to extrusion and shaping at from 50°C to 180°C. This melt extrusion type of process, as described above, is disclosed in US 6,365,188. Whereas the inventors of US 6,365,188 were apparently aware of melt extrusion processes using a polymeric binder, they did not envisage inclusion of polymeric binders into the

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cyclodextrin/active ingredient mixture of US 6,365,188. The aforementioned thus provides evidence that the skilled artisan, with knowledge of the cited art references, would have not been motivated to combine US 4,801,460 and US 6,365,188. In fact, the skilled person would have expected that "dilution" of the cyclodextrin/active ingredient mixture by 50-98% by weight of a polymeric binder would effect the desired interaction of cyclodextrin and active ingredients and teach away from their combination.

Accordingly, because US 6,365,188 in combination with US 4,801,460, fail to teach, suggest or disclose all the limitations of the claimed invention, 1) mixing and plasticizing ... at a temperature below 170°C, and 2) 50 to 98% by weight of the at least one polymeric binder, *prima facie* obviousness has not been established. Therefore, applicants respectfully request withdrawal of the 103 rejection.

Claims 1-7 stand rejected over US 6,365,188 in view of US 6,046,177. Applicants canceled claim 1 and amended claims 2-7 to depend from claim 8. Claim 8 stands free of an obviousness rejection based on the above mentioned cited art combination. Accordingly, the rejection is moot and Applicants respectfully request its withdrawal.

In sum, the overall disclosures, teachings, and suggestions of the prior art, and the level of skill in the art - i.e., the understandings and knowledge of persons having ordinary skill in the art at the time of the invention - fail to support the legal conclusion of obviousness. Accordingly, for at least the reasons listed above, it would not have been obvious to combine US 4,801,460 and US 6,365,188. Thus, a *prima facie* case of obviousness has not been established by the Examiner, and the rejection under 35 USC §103 should be withdrawn. Favorable action is solicited.

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Conclusion

Applicants respectfully submit that the present application is in condition for allowance, which action is courteously requested. Please charge any shortage in fees due in connection with the filing of this paper to Deposit Account 14.1437. Please credit any excess fees to such account.

Respectfully submitted,



Todd R. Samelman
Registration No.: 53,547

NOVAK DRUCE & QUIGG, LLP
Customer No.: 26474
1300 Eye St. N.W.
400 East Tower
Washington, D.C. 20005
Phone: (202) 659-0100
Fax: (202) 659-0105